

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43*bis*.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/GB2005/050002

International filing date (day/month/year)  
06.01.2005

Priority date (day/month/year)  
08.01.2004

International Patent Classification (IPC) or both national classification and IPC  
A61K31/505, C07D239/54, C07F7/08, A61P33/00, A61P33/06

Applicant  
MEDIVIR AB

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

10/585283  
IP20 Rec'd PCT/PTO 03 JUL 2006  
International application No.  
PCT/GB2005/050002

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating there has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. II Priority**

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1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, when required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

WRITTEN OPINION OF THE  
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial  
applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 19

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 19
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
  - the written form ☐ has not been furnished
  - ☐ does not comply with the standard
  - the computer readable form ☐ has not been furnished
  - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

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**Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or  
Industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-13,16
	No: Claims	14,15,17,18,20-26
Inventive step (IS)	Yes: Claims	1-13,16
	No: Claims	14,15,17,18,20-26
Industrial applicability (IA)	Yes: Claims	1-18,20-26
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)

PCT/GB2005/050002

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Re Item III.

Claim 19 is missing in the application

Re Item V.

1 Reference is made to the following documents:

- D1 : PATENT ABSTRACTS OF JAPAN vol. 012, no. 283 (C-518), 3 August 1988 (1988-08-03) & JP 63 060929 A (YODOGAWA SEIYAKU KK), 17 March 1988 (1988-03-17)
- D2 : PATENT ABSTRACTS OF JAPAN vol. 012, no. 022 (C-470), 22 January 1988 (1988-01-22) & JP 62 174011 A (TAKEDA CHEM IND LTD), 30 July 1987 (1987-07-30)
- D3 : PATENT ABSTRACTS OF JAPAN vol. 012, no. 438 (C-544), 17 November 1988 (1988-11-17) & JP 63 165373 A (YODOGAWA SEIYAKU KK), 8 July 1988 (1988-07-08)
- D4 : US 5 859 014 A (BANTLE ET AL) 12 January 1999 (1999-01-12)
- D5 : SKARIC, VINKO ET AL. "Homologation and intramolecular cyclization reactions in aliphatic deoxyuridine analogs series" CROATICA CHEMICA ACTA, 56(1), 125-39 CODEN: CCACAA; ISSN: 0011-1643, 1983, XP008047706
- D6 : WO 95/18820 A (ISIS PHARMACEUTICALS, INC; COOK, PHILLIP, DAN; AGEVEDO, OSCAR, L, DAVI) 13 July 1995 (1995-07-13)
- D7 : WO 93/02044 A (BAKER CUMMINS PHARMACEUTICALS, INC) 4 February 1993 (1993-02-04)
- D8 : EP 0 748 800 A (F. HOFFMANN-LA ROCHE AG) 18 December 1996 (1996-12-18)

2 CLAIMS 14,15,17,18,20-26

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,15,17,18,20-26 is not new in the sense of Article 33(2) PCT.

Document D1 discloses (see the passages cited in the search report)

1-[[2-[bis(4-methoxyphenyl)phenylmethoxy]-1-(hydroxymethyl)ethoxy]methyl]-5-fluoro-2,4(1H,3H)-pyrimidinedione and 1-[[1-[[bis(4-methoxyphenyl)phenylmethoxy]methyl]-2-[(3-methyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy]ethoxy]methyl]-2,4(1H,3H)-pyrimidinedione as compounds that are used as antitumor agents.

- 2.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,17,18,20,23-26 is not new in the sense of Article 33(2) PCT.

Document D2 discloses (see the passages cited in the search report) 1-[2-methoxy-3-(triphenylmethoxy)propyl]-3-[2-(phenylmethoxy)ethyl]-2,4(1H,3H)-Pyrimidinedione, 1-[2-methoxy-3-(triphenylmethoxy)propyl]-3-(2-pyridinylmethyl)-2,4(1H,3H)-Pyrimidinedione and 1-[2-methoxy-3-(triphenylmethoxy)propyl]-2,4(1H,3H)-Pyrimidinedione and their use as antitumor agents

- 2.3 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,15,17,18,20,21,23-26 is not new in the sense of Article 33(2) PCT.

Document D3 discloses (see the passages cited in the search report) (1R) 1-[[1-[[bis(4-methoxyphenyl)phenylmethoxy]methyl]-2-[(3-methyl-1,3,2-oxazaphospholidin-2-yl)oxy]ethoxy]methyl]-2,4(1H,3H)-pyrimidinedione; 1-[[1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-2-[(3-methyl-1,3,2-oxazaphospholidin-2-yl)oxy]ethoxy]methyl]-2,4(1H,3H)-pyrimidinedione; 1-[[2-[bis(4-methoxyphenyl)phenylmethoxy]-1-(hydroxymethyl)ethoxy]methyl]-2,4(1H,3H)-pyrimidinedione; and 1-[[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(hydroxymethyl)ethoxy]methyl]-2,4(1H,3H)-pyrimidinedione per se and as antiviral or antitumor agents.

- 2.4 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,15,17,18,20 is not new in the sense of Article 33(2) PCT.

Document D4 discloses (see the passages cited in the search report) 1-[2-(Trimethylsilyl)ethoxymethyl]-2,4(1H,3H)-pyrimidinedione and 3-(3-chloropropyl)-1-[2-(trimethylsilyl)ethoxymethyl]-2,4(1H,3H)-pyrimidinedione as compounds per se.

- 2.5 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,18,20,23-25 is not new in the sense of Article 33(2) PCT. Document D5 discloses (see the passages cited in the search report) 1-(3-O-triphenylmethyl-2,3-dihydroxypropyl)uracil and 1-(-2-O-methylsulfonyl-3-O-triphenylmethyl-2,3-dihydroxypropyl)uracil.
- 2.6 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,17,18,23-25 is not new in the sense of Article 33(2) PCT. Document D6 discloses (see the passages cited in the search report) 1-(1-Uracil)-3-O-dimethoxytrityl-2-propanol as compound per se.
- 2.7 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,15,18,20,21,25 is not new in the sense of Article 33(2) PCT. Document D7 discloses (see the passages cited in the search report) 1-[[2-(tert-butyldimethylsilyl) oxy]ethoxy] methyl]uracil.
- 2.8 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 14,15,17,18 is not new in the sense of Article 33(2) PCT. Document D8 discloses (see the passages cited in the search report) 1-[2-(Trimethylsilyl)ethoxymethyl]-2,4(1H,3H)-pyrimidinedione.
- 3 CLAIMS 14,15, 17, 18, 20-26  
Dependent claims 14, 15, 17, 18, 20-26 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT).